REMARKS

Claims 122, 178 and 185-232 are pending, with claims 122, 185, 189, 192, 197, 200, 221-224, 226 and 228-232 being under consideration. Claim 178 is withdrawn as directed to a non-elected invention, and claims 186-188, 190, 191, 193-196, 198, 199, 225 and 227 are withdrawn as directed to a non-elected species.

Claims 122, 178 and 190-220 have been amended solely for purposes of clarity and proper antecedent basis. No new matter has been added.

Applicants request that the amendments and remarks made herein be entered and made of record in the file of the above-identified application.

I. STATEMENT OF SUBSTANCE OF INTERVIEW UNDER 37 C.F.R. § 1.133

Pursuant to 37 C.F.R. § 1.133 and MPEP 713.04, Attorneys for Applicant submit this Interview Summary in connection with the telephonic interview of January 29, 2009 between Examiner Mark Staples, Primary Examiner Kenneth Horlick, Eileen Sun, and Attorneys for Applicants, Adriane Antler and Maya Elbert, in connection with the above-identified application.

During the telephonic interview, the following rejections in the Office Action were discussed: the rejection of claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226 and 228-232 under 35 U.S.C. § 103(a) over U.S. Patent No. 6,329,140 to Lockhart ("Lockhart") in view of Bowtell, 1999, Nature Genetics Supplement 21:25-32 ("Bowtell") and U.S. Patent No. 6,013,436 to Hui *et al.* ("Hui"); and the rejection of claim 223 under 35 U.S.C. § 103(a) over Lockhart, Bowtell and Hui, and further in view of Schena. Dr. Antler presented reasons why the claimed invention was non-obvious, essentially as set forth in the remarks below.

In particular, Dr. Antler emphasized that the use of probes complementary to sequences contained entirely within an intron is not properly combinable with expression arrays such as taught by Bowtell or Schena, since such intron probes are inoperable in expression analyses because they do not hybridize to sequences expressed into proteins such as cDNA. In support, Dr. Antler cited *In re Gordon*, 773 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984) and MPEP 2143.01 (V), 8th Edition August 2001 (Revision of July 2008). Dr. Antler further pointed out that one of ordinary skill in the art would not have a reason to combine the disparate elements of large span, high density, and such intron probes, because

there was no appreciation in the art that such would provide the utility afforded by the present invention, *i.e.*, that such would provide a high throughput useful way of identifying exon structure across the genome.

The Examiners stated that Applicants' points were well taken, and that they would reconsider the rejections in view of Applicants' arguments.

II. THE REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

The previous rejection of claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226 and 228-232[1] under 35 U.S.C. § 103 as obvious over U.S. Patent No. 6,329,140 to Lockhart ("Lockhart") in view of Bowtell, 1999, Nature Genetics Supplement 21:25-32 ("Bowtell") was withdrawn by the Examiner. The rejection of claim 223 as obvious over Lockhart and Bowtell, and further in view of Schena *et al.*, 1996, Proc. Natl. Acad. Sci. U.S.A. 93:10614-19 ("Schena") was also withdrawn by the Examiner. However, the Examiner issued a new rejection of claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226 and 228-231[2] under 35 U.S.C. § 103 as obvious over Lockhart, Bowtell and U.S. Patent No. 6,013,436 to Hui *et al.* ("Hui"). The Examiner also issued a new rejection of claim 223 as obvious over Lockhart, Bowtell and Hui, and further in view of Schena. Applicants respectfully disagree with the new rejections, for the reasons discussed below.

A. Legal Standard

In *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q. 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 127 S.Ct. at 1734, 82 U.S.P.Q.2d at 1388 (quoting *Graham*, 383 U.S. at 17-18, 14 U.S.P.Q. at 467).

In order to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). Additionally, the Supreme Court, in *KSR*, affirmed that "a

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[1] The Examiner omitted claim 232 from the statement of the rejection under 35 U.S.C. §103 on page 2 of the Office Action, apparently inadvertently.

[2] The Examiner omitted claim 232 from the statement of the rejection under 35 U.S.C. §103 on page 3 of the Office Action, apparently inadvertently.

patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art," and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. In addition, under *KSR*, "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR*, S.Ct. at 1740, 82 U.S.P.Q.2d at 1396.

Further, hindsight should be avoided in applying the nonobviousness requirement. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed. Cir. 1987), *cert. denied*, 481 U.S. 1052 (1987). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988). Moreover, a recent post-*KSR* Federal Circuit decision explained that a non-rigid "flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis" and assures that the obviousness test proceeds on the basis of evidence that arise before the time of invention as the statute requires. *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364-65 (Fed. Cir. 2008) (citing *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

Finally, in considering a prior art reference, the reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 U.S.P.Q. 769, 779 (Fed. Cir. 1983). A proposed modification that renders a prior art invention inoperable for its intended purpose cannot support an obviousness rejection. *See In re Gordon*, 773 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984). *See also* MPEP 2143.01 (V), 8th Edition August 2001 (Revision of July 2008).

B. Independent Claim 122 and Claims 185, 189, 192, 197, 200, 221, 222, 224, 226, and 228-232 Depending Therefrom Are Patentable Over Lockhart, Bowtell and Hui.

The presently claimed invention relates to positionally-addressable ordered arrays of polynucleotide probes bound to a solid support, wherein the polynucleotide probes comprise at least 100 polynucleotide probes of different nucleotide sequences, each said different nucleotide sequence comprising a sequence complementary and hybridizable to a different genomic sequence of the same species of organism, wherein the respective genomic sequences complementary and hybridizable to the probes are found at sequential sites in the genome. The claimed arrays are characterized by the following three essential features: (1) a high density of the genomic sequences complementary to probes in the genome (because the distance between 5′ ends of the sequential sites is always less than 500 bp), (2) a large span of the genomic sequences (because the genomic sequences complementary and hybridizable to the probes span a genomic region of at least 25,000 bp), and (3) at least two probes complementary and hybridizable to genomic sequences contained entirely within an intron (which intron can be the same intron or different introns for the respective at least two probes). It is noted that feature (3) specifies probes to sequences that are contained entirely within introns and thus do not overlap exon sequences. Accordingly, in the discussion below, such probes are referred to as "Exclusively Intron Probes."

The Examiner has relied on Bowtell for the large span of Applicants' claims, on Lockhart for the high density of the claims, and on Hui for allegedly teaching the Exclusively Intron Probes of the claims. However, there is no discernible reason that would have prompted a person of ordinary skill in the relevant field to combine the elements disclosed in Bowtell, Lockhart and Hui in the way that Applicants' invention does. *See KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. Furthermore, such combination would render the intron probes of Hui inoperable for their intended purpose. *See In re Gordon*, 221 U.S.P.Q. at 1127. The foregoing is elaborated in detail below.

Bowtell discloses use of microarray probes, representing expressed sequences – ORFs, cDNAs or ESTs, to analyze expression of genes into proteins, wherein the probes span a large region of the genomic sequence (see Bowtell at page 29, Table 3, columns 1 and 2). Thus, Bowtell's arrays have the feature of a large span, but not the high density or Exclusively Intron Probes of the claims. Bowtell deals solely with expression analysis, and thus, Bowtell is not concerned with probing any genomic sequences that are not expressed

into proteins. Thus, it would run counter to common sense based on Bowtell to use Exclusively Intron Probes, because the use of such probes does not detect protein expression. Therefore, using probes that hybridize to sequences contained entirely within an intron (*i.e.*, Exclusively Intron Probes) in the arrays of Bowtell would render the Exclusively Intron Probes inoperable for the intended purpose of Bowtell and inoperable for the provision of any useful information since such probes would not hybridize to the protein-coding sequences (*e.g.*, cDNAs or mRNAs, see Bowtell at, *e.g.*, p. 26, left col., 1st para) with which expression arrays are contacted, and thus yield no information about such expressed sequences. *See In re Gordon*, 221 U.S.P.Q. at 1127. Thus, placing Exclusively Intron Probes in Bowtell's array would not provide any useful function and would be counter to common sense.

Lockhart discloses use of tiling arrays to determine whether a given gene possesses a sequence signature of up to 300 nucleotides or up to 300 amino acids in order to obtain information about the given gene, *e.g.*, to determine whether it encodes a member of a gene family or comprises a sequence from one of a set of genes (see Lockhart at Abstract, column 1, lines 50-59 and column 7, line 10 to column 8, line 12). There is no disclosure or suggestion in Lockhart that such sequence signatures may be located within introns or may span at least 25,000 bp. In response to Applicants' previous arguments that probes to introns are not taught in Lockhart, the Examiner states that: (1) Lockhart does not exclude probes to introns, (2) claim 1 of Lockhart is not limited to probing polynucleotides which encode polypeptides, and (3) Hui is relied upon for the teaching of intron probes (Office Action at page 4). Applicants address each of these three points in turn below.

First, although Lockhart does not exclude probes to introns, such failure to exclude is not a proper basis to support an obviousness rejection. Under the standard enunciated by the Supreme Court in *KSR*, a determination of obviousness requires a reason to combine the component elements of the cited references, which this first point does not provide.

Second, Applicants agree that Lockhart is not limited to probing signature sequences that encode polypeptides. Accordingly, Applicants will address both the "coding" and "noncoding" embodiments of Lockhart: (i) embodiments that probe coding nucleotide sequences expressed into proteins that contain sequence signatures of interest, and (ii) embodiments that probe non-coding nucleotide sequences that contain sequence signatures of interest (*e.g.*, a Hogness box, a TATA box, a homeobox; see Lockhart at col. 7, lines 44-46). In the first type of embodiments, where Lockhart teaches probing for signature sequences in

expressed protein sequences, it would be nonsensical to use Exclusively Intron Probes which do not recognize any coding sequences, much less coding sequences containing a sequence signature of interest. Furthermore, in such embodiments, Lockhart teaches probing coding regions and to avoid probing regions that are near expected intron/exon boundaries:

> The interrogated regions were chosen based on a few criteria: they include regions that are (a) reasonably well conserved (highly conserved at the amino acid level, but less so at the DNA level) and that serve as identifiers of the protein family, (b) highly variable and serve as unique identifiers of individual members of the family, and (c) not near expected intron/exon boundaries.

(see Lockhart at col. 27, lines 11-17, emphasis added). Thus, in such embodiments, not only is there no reason to use probes to introns, but Lockhart teaches away from probing even near intron/exon boundaries. Moreover, using the Exclusively Intron Probes in the arrays of Lockhart that probe for sequence signatures in coding sequences would render the Exclusively Intron Probes inoperable for the intended purpose of such arrays of Lockhart, because intron probes do not hybridize to coding sequences, and thus yield no information about such sequences. *See In re Gordon*, 221 U.S.P.Q. at 1127. As discussed above for Bowtell, using such Exclusively Intron Probes in the arrays of Lockhart would serve no useful function and would be counter to common sense, since the Exclusively Intron Probes would not hybridize to the coding nucleic acids with which Lockhart's protein sequence signature arrays would be contacted.

The second type of embodiments, in which Lockhart teaches tiling across sequence signatures that are not expressed as proteins, has no relevance to and cannot properly be combined with the teachings of Bowtell, which deals solely with protein expression analysis. Furthermore, even in its non-coding embodiment, Lockhart does not disclose using any intron probes, much less at least two probes contained entirely within an intron, *i.e.*, the Exclusively Intron Probes, recited in Applicants' claims.

Third, the Examiner relies on Hui for allegedly supplying the third essential element of Applicant's claims—at least two probes contained entirely within an intron, *i.e.*, the Exclusively Intron Probes. Hui is interested in diagnosing mutations in one specific gene: the von Hippel-Lindau ("VHL") tumor suppressor gene. Hui discloses oligonucleotides

complementary to intron regions, and particularly regions immediately flanking intron/exon boundaries, of the VHL tumor suppressor gene for use as amplification and sequencing primers in the diagnosis of VHL gene mutations (see Hui at col. 3, line 8 to col. 4, line 16). Hui does not teach or suggest that such oligonucleotides complementary to intron regions are immobilized on an array. Hui also teaches use of a panel of probes for various known mutations in the VHL tumor suppressor gene immobilized as an array on an avidin or streptavidin support to be probed with patient DNA (see Hui at col. 10, lines 52-54). Hui does not teach that probes to mutations in the VHL intron sequences be used. In addition, Hui's arrays lack the large span and high density of the claimed invention.[3] However, even assuming *arguendo* that Hui did disclose the use of Exclusively Intron Probes on an array, combining such disclosure with Lockhart[4] at most still provides an array with Exclusively Intron Probes and high density that lacks the large span of the claims. Moreover, such an array cannot properly be combined with Bowtell to provide the large span of the claims because, as discussed above, combining such Exclusively Intron Probes with the expression arrays of Bowtell runs counter to common sense and renders the Exclusively Intron Probes inoperable for the intended purpose of Bowtell and for any useful function since Exclusively Intron Probes will not hybridize to the cDNAs (or mRNAs) with which expression arrays are contacted, and will not hybridize to sequences expressed as proteins. See *In re Gordon*, 221 U.S.P.Q. at 1127.

Additionally, there is no other reason that would motivate one of ordinary skill in the art to combine the disparate features of large span, high density and Exclusively Intron Probes to achieve the claimed invention, because there was no appreciation or recognition in

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[3] Hui does not teach or suggest the large span feature of the claimed arrays, since Hui is interested in identification of mutations in only one gene – the VHL tumor suppressor gene, which has a span of only 10,741 bp. *See* "Homo Sapiens gene VHL, encoding von Hippel-Lindau tumor suppressor," NCBI, AceView [online], [retrieved on 12/30/2008]. Retrieved from the Internet: <URL: http://www.ncbi.nlm.nih.gov/IEB/Research/Acembly/av.cgi?db=human&c=Gene&l=VHL>, made of record as Ref. C252 in the Supplemental Disclosure Statement submitted herewith. Hui does not teach or suggest the high density of the claimed arrays, since Hui is interested only in probing for various known mutations in the VHL tumor suppressor gene, and thus, probing only at predetermined sites in this gene.

[4] Hui properly at most can be combined only with the non-coding embodiment of Lockhart, because, as discussed above, it is contrary to common sense to use the Exclusively Intron Probes in an embodiment of Lockhart relating solely to signature sequences expressed as proteins, since the Exclusively Intron Probes do not hybridize to sequences that are expressed as proteins.

the art that such would serve any useful purpose. In contrast, it was the instant invention which recognized that the presently claimed arrays, by virtue of their large span, high density, and Exclusively Intron Probes, give rise to a new function that is not afforded by the elements of Bowtell, Lockhart and Hui relied on by the Examiner. The claimed arrays provide a high throughput method to determine the structure of genes and to precisely identify the boundaries of expressed genes in genomic sequences, for example by delineating intron/exon boundaries, without extensive DNA sequencing of ESTs (see specification at page 3, lines 13-28 and page 4, lines 1-21). The arrays, which span a genomic region of at least 25,000 bp, wherein the distance between 5' ends of said sequential sites is always less than 500 bp, and wherein the nucleotide sequences of at least two of the probes are complementary and hybridizable to genomic sequences contained entirely within an intron, allow one to rapidly gather high resolution information about location and structure of genes even if exons of genes are spread over large regions of the genome, including location of introns and intron/exon boundaries. Thus, the microarrays of the present invention enable an efficient and comprehensive genome scan that provides much more detailed data than prior art methods.

Based on the foregoing, one of ordinary skill in the art would not be prompted to combine the teachings of Bowtell with either the teachings of Lockhart or the teachings of Hui. As set forth in *KSR*, it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...." *KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. In the instant case, such a reason is not present, because the cited references simply do not provide a common sense reason for such combination. To the contrary, as explained above, there is reason not to combine the individual elements of the cited references in the manner proposed by the Examiner.

In a post-*KSR* decision, the Court of Appeals for the Federal Circuit declared that a "flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis" and assures that the obviousness test proceeds on the basis of evidence that arises before the time of invention as the statute requires; however, none of the three cited references contain any reason under this flexible test to combine the elements taught in these references as proposed by the Examiner. See *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364-65 (Fed. Cir. 2008) (citing *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007)). Accordingly, Applicants submit that the combination of cited references set forth in the

Office Action is indicative of the fact that the Examiner has relied on Applicant's own disclosure as the basis for formulating such combination rejection, constituting an impermissible reliance on hindsight gained from Applicant's own specification. Without such benefit of hindsight, the teachings of the references cited by the Examiner, alone or in combination, could not possibly render obvious the claimed invention. The Federal Circuit has affirmed that "one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988).

It is evident that the arrays of the claims are "more than the predictable use of prior art elements according to their established functions." *See KSR*, 127 S.Ct. at 1740 (citing *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57 (1969) and *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273 (1976)). Specifically, the claimed arrays are more than the predictable use of the elements of Lockhart, Bowtell and Hui according to their established functions. As described above, Lockhart uses tiling arrays for signature sequence identification, thereby identifying gene family members having a particular sequence signature, and, as discussed above, teaches away from probing regions near intron/exon boundaries, and thus, teaches away from the function of precisely identifying the boundaries of expressed genes in genomic sequences afforded by the Applicants' invention. Bowtell uses arrays having a large span solely to determine whether genes are expressed into proteins, and Hui uses arrays with probes to known mutations in a specific gene, the VHL tumor suppressor gene, to diagnose disease-associated mutations. In contrast, the Applicant's invention provides a high throughput method to determine the structure of genes as described above. Thus, the claimed invention does not employ known elements according to their established functions.

Therefore, claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226 and 228-232 are not made obvious by Lockhart, Bowtell and Hui, and the rejection of these claims should be withdrawn.

Regarding claim 185, Applicants further note that, in contrast to the Examiner's assertion regarding claim 185 on page 4 of the Office Action, Lockhart does not teach that one can exclude "low information content selected from the group consisting of repetitive elements, simple repeats, and polyX repeats" as specified in Applicants' claim 185. The Examiner cites Lockhart at col. 12, lines 7-12 to support the proposition that Lockhart teaches that one can exclude low information content, however, the cited paragraph of Lockhart

simply states that "the process can be repeated using different arrays having different sets of sequence signatures until the desired level of detail regarding the sequence of the target nucleic acid is obtained." In the cited paragraph, Lockhart explains that a target nucleic acid may be tested a number of times each time using arrays of probes directed to a different set of sequence signatures. The cited paragraph does not address the issue of exclusion of low information content sequences. Applicants further point out that the specification does provide a clear description of the term "low information content," so as to make the meaning of the term clear. Specifically, Applicants direct the Examiner's attention to page 16, line 31 to page 18, line 9 of the originally filed specification for the thorough description of such low information content elements and the methods for their exclusion. Furthermore, regions of low information content include repetitive elements (see claim 185 and specification at page 16, line 33), and Lockhart teaches that repeat sequences may comprise a sequence signature (see Lockhart, *e.g.*, at col. 11, lines 43-45), and thus suggests that such sequences should not be excluded. Consequently, not only does Lockhart not teach or suggest the limitation of claim 185, but Lockhart teaches away from such limitation.

C. Claim 223 Is Patentable Over Lockhart, Bowtell And Hui in View of Schena

Finally, with respect to claim 223, the Examiner relies on Schena for its disclosure of microarrays to measure expression of plant genes to support the alleged obviousness of claim 223 (Office Action at page 8). Specifically, the Examiner asserts that it would have been obvious to one skilled in the art to modify the array of Lockhart, Bowtell and Hui by targeting nucleotide sequences of plant genes as suggested by Schena because Schena teaches usefulness of microarrays in measuring plant genes and Lockhart, Bowtell and Hui teach the detection of genes and gene mutations using arrays and microarrays (Office Action at pages 8-9).

Claim 223 is not obvious over Bowtell, Lockhart, Hui and Schena by virtue of its dependency on claim 122, which is not obvious over any of these references alone or in combination, for the reasons discussed above. Applicants point out that Schena suffers from the same deficiencies as Bowtell, and there is no discernible reason that would have prompted a person of ordinary skill in the art to combine Schena with Lockhart and Hui to create an array with a probe set having the long span, high density, and at least two probes that are hybridizable to genomic sequences contained entirely within an intron, as specified in Applicants' claims.

Like Bowtell, Schena is directed to the analysis of gene expression into proteins, in Schena's case using cDNAs as probes. Schena is concerned with the use of microarrays containing 1046 random human cDNA clones from a library of Epstein-Barr virus-transformed human peripheral blood lymphocytes, with 10 *Arabidopsis* clones as controls, for monitoring gene expression into proteins (see Schena at page 10614, under "Materials and Methods"). Schena also discloses use of microarrays of cDNA clones to measure expression of plant genes (see Schena at page 10614, left column). There is no reason based on Schena to probe for intron sequences. Further, using probes contained entirely within an intron (*i.e.*, Exclusively Intron Probes) in the arrays of Schena would render the Exclusively Intron Probes inoperable for the intended purpose of Schena and for any useful function, because intron probes do not hybridize to the protein-coding sequences with which expression arrays are contacted, and thus do not detect gene expression into proteins. Using such Exclusively Intron Probes in Schena's expression arrays would be counter to common sense, since the Exclusively Intron Probes would not hybridize to the coding sequences with which such expression arrays are contacted. A proposed modification that renders a prior art invention inoperable for its intended purpose cannot support an obviousness rejection. *See In re Gordon*, 221 U.S.P.Q. at 1127. On the other hand, Hui is concerned solely with detection of known mutations in the VHL gene and is not concerned with probing a large region of the genome to analyze gene expression into proteins. Thus, there is no discernible reason based on Hui to use microarrays utilizing cDNA probes spanning a large genomic sequence as taught in Schena (see Schena at page 10614, under "Materials and Methods"). Further, it would run counter to the purpose of Hui because Hui is only interested in one gene, the VHL tumor suppressor gene. *See In re Gordon*, 221 U.S.P.Q. at 1127. Lockhart does not remedy this deficiency because it provides no reason to use the Exclusively Intron Probes in expression arrays.

Additionally, there is no other reason that would motivate one of ordinary skill in the art to combine Bowtell, Schena, Lockhart and Hui, for the same reasons as discussed above.

Therefore, claim 223 is not made obvious by Lockhart, Bowtell, Hui and Schena, and the rejection of claim 223 should be withdrawn.

In view of the foregoing remarks, it is submitted that the obviousness rejections are in error and should be withdrawn.

III. CLAIMS WITHDRAWN FROM CONSIDERATION AS BELONGING TO NON-ELECTED SPECIES SHOULD BE CONSIDERED

Claims 186-188, 190-191, 193-196, 198-199, 201-220, 225 and 227 were withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claims are allowable, claims 186-188, 190-191, 193-196, 198-199, 201-220, 225 and 227 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants respectfully request that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney if a telephone call would help resolve any remaining items.

Respectfully submitted,

Date: February 26, 2009

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